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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/715,418	11/16/2000	David A. Lewin	10716/12	7715

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EXAMINER	
ROMEO, DAVID S	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 06/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/715,418	LEWIN ET AL.	
	Examiner	Art Unit	
	David S. Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45,47-49,61-63 and 65-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45,47-49,61-63 and 65-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

The amendment filed 03/18/2005 has been entered. Claims 45, 47-49, 61-63, 65-67 are pending and being examined.

The drawings were received on 03/18/2005. These drawings are acceptable.

Maintained Formal Matters, Objections, and/or Rejections:

Claim Rejections - 35 USC § 112

Claims 45, 47-49, 61-63, 65-67 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Applicants argue that "beyond a reasonable doubt" and "statistical certainty" are not the appropriate standards for judging utility. Applicants argue that the appropriate standard is "more likely than not." Applicants argue that the claimed invention is useful for the detection of misregulation of the Wnt-1 pathway, which has been implicated in the transformation of cells into colon, breast, and ovarian tumors. Applicants argue that the correlation between the source of SEQ ID NO: 3 and its human ortholog expressed in human cancer cells demonstrates that SEQ ID NO: 3 has utility for detection of transformed cells and that sufficient nexus is described between SEQ ID NO: 3 and cancer to provide a credible utility. Applicant's arguments have been fully considered but they are not persuasive. The present rejection is not based upon a "statistical certainty" or "proof beyond a reasonable doubt." The present rejection is based upon Applicants' failure to disclose to disclose enough information about the invention to make its

usefulness immediately apparent to those familiar with the technological field of the invention. The M.P.E.P. reminds Office personnel that they must treat as true a statement of fact made by an applicant in relation to an asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement. Applicants have not presented any evidence regarding the role, expression or activity of SEQ ID NO: 3, i.e., the claimed invention. Applicants have not shown that SEQ ID NO: 3 is overexpressed in any tumors in which Wnt-1 is spontaneously misregulated. Furthermore, there is an inherent lack of certainty in predicting protein levels from mRNA levels, as shown by Haynes and Allman. The skilled artisan would have a reasonable, legitimate basis to doubt the utility of the SEQ ID NO: 3 polypeptide because the skilled artisan recognizes that protein levels are not always consistent with mRNA levels. The evidence, considered as a whole, provides a reason for one skilled in the art to question the objective truth of the statement of diagnostic or therapeutic use of the claimed polypeptides. In the absence of any information on the role, activity, or expression of SEQ ID NO: 3 in cancer, the examiner considers the asserted utilities to not be specific and substantial because the skilled artisan would not know if SEQ ID NO: 3 expression would be upregulated, down-regulated, or unchanged in cancer.

Applicants argue that mRNA expression is commonly used to analyze protein activity, that the primary role of RNA transcripts is to serve as templates for protein synthesis, that Haynes, Hancock, and Allman provide no teaching that would discredit an association between expression of a polynucleotide encoding SEQ ID NO: 3 and expression of SEQ ID NO: 3, nor between SEQ ID NO: 5 expression and SEQ ID NO: 6 expression. Applicant's arguments have been fully considered but they are not persuasive. Haynes, Hancock, and Allman do provide a

teaching that mRNA levels are not necessarily consistent with protein levels and the present application doesn't provide any data regarding the expression levels of the SEQ ID NO: 3 or SEQ ID NO: 6 polypeptides in cancer cells or normal cells. .

Applicants argue that Haynes, Hancock, and Allman can also be interpreted as supporting the general correlation between mRNA and protein expression because Haynes "found a general trend," which supports an assertion that a correlation between mRNA expression and protein expression is more likely than not true. Since the instant claims are directed to the SEQ ID NO: 3 polypeptide, it is reasonable to consider whether the skilled artisan would have a reasonable basis to question the asserted utilities of the SEQ ID NO: 3 polypeptide based solely on the differential analysis of SEQ ID NO: 2 mRNA expression. Haynes was cited as providing evidence that protein expression levels are not predictable from the mRNA expression levels. Haynes cites this lack of predictability as one of the main reasons for proteome analysis to become an essential component in the comprehensive analysis of biological systems. Paragraph bridging pages 1862-1863; page 1863, left column, full paragraph 1. Haynes further teaches that "it is evident that the analysis of mature protein products in cells is essential as there are numerous levels of control of protein synthesis, degradation, processing and modification, which are only apparent by direct protein analysis" page 1863, right column, full paragraph 2). Haynes, considered as a whole, teaches that protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript and that there are numerous levels of control of protein synthesis, degradation, processing and modification, which are only apparent by direct protein analysis. Thus, Haynes supports the examiner's position that the skilled artisan would not know if a change in mRNA level is associated with a corresponding change in protein levels and that

the skilled artisan would have a legitimate basis to doubt the utility of the SEQ ID NO: 3 polypeptide because the skilled artisan would not know if SEQ ID NO: 3 expression would be upregulated, down-regulated, or unchanged in cancer. One skilled in the art would be required to do further research in order to determine whether or not the claimed polypeptide levels changed significantly in the tumor samples. Such a further research requirement makes it clear that the asserted utility is not yet in currently available form, i.e., it is not substantial. This further experimentation is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete.

Applicants argue that Hancock does not discredit the relationship between mRNA and protein expression. Applicant's arguments have been fully considered but they are not persuasive. Applicants' statement regarding Hancock is merely conclusory. Hancock is consistent with Haynes. Namely, the analysis of protein products is essential because protein expression levels are not predictable from the mRNA expression levels. One skilled in the art would be required to do further research in order to determine whether or not the claimed polypeptide levels changed significantly in the tumor samples. Such a further research requirement makes it clear that the presently asserted utilities are not yet in currently available form, i.e., they are not substantial.

Applicants argue that Allman has no relationship to the present application and makes no suggestion of a lack of a correlation between mRNA expression and protein expression. Applicant's arguments have been fully considered but they are not persuasive. Allman clearly notes the discordance between Bcl-6 mRNA expression and Bcl-6 protein expression (Abstract).

Applicants argue that SEQ ID NO: 3 can be used to test for agents that can inhibit overexpression of SEQ ID NO: 3. Applicants argue that that SEQ ID NO: 3 can be used to make antibodies and that those antibodies can be used to detect or treat cancers expressing human orthologs. Applicants discussion of paragraph 6 of the utility guidelines is noted. Applicants' arguments have been fully considered but they are not persuasive. In the absence of any data regarding the expression, role, or activity or SEQ ID NO: 3 and in the presence of data that protein levels cannot be predicted from mRNA levels, there is no basis for concluding that the skilled artisan would be convinced that it is more likely than not that SEQ ID NO: 3 could be used for the diagnosis or treatment of cancer.

Claims 45, 47-49, 61-63, 65-67 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. As Applicants recognize, a rejection under § 112, first paragraph, may be maintained on the same basis as a lack of utility rejection under § 101. A deficiency under 35 U.S.C. 101 also creates a deficiency under 35 U.S.C. 112, first paragraph. If the application fails as a matter of fact to satisfy 35 U.S.C. § 101, then the application also fails as a matter of law to enable one of ordinary skill in the art to use the invention under 35 U.S.C. § 112. Obviously, if a claimed invention does not have utility, the specification cannot enable one to use it. As such, a rejection properly imposed under 35 U.S.C. 101 should be accompanied with a rejection under 35 U.S.C. 112, first paragraph. The 35 U.S.C. 112, first paragraph, rejection set out a separate rejection that incorporates by reference the

factual basis and conclusions set forth in the 35 U.S.C. 101 rejection. A 35 U.S.C. 112, first paragraph, rejection should be imposed or maintained when an appropriate basis exists for imposing a rejection under 35 U.S.C. 101.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571) 272-0961.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-8300.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (571) 273-0890.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

David Romeo

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
MAY 27, 2005